REMARKS

1. Claim Amendments

Claim 1 previously provided (I) "covalently linking said anti-codons **and/or**" (II) covalently linking the at least one template with the anti-codon of at least one building block. (The "(I)" and "(II)" are not part of the claim but were merely added for reference below.)

Claim 1 thus read on three embodiments,

-- (I) not (II)

-- (II) not (I)

-- (I) and (II).

By this amendment, we make (I) mandatory, thus eschewing the second of the three embodiments.

Consequently, the claim was rewritten into the form (I) "and optionally" (II), with basis in the original claim.

For greater clarity we replace "covalently linking said anti-codons" with --covalently linking each of said anti-codons with at least one other anti-codon--, to make it clearer what they are linked to. For basis see e.g. P14, L4-6.

Certain "optional" language has been deleted from clause (a) of claim 1. Since it was optional, it plainly can be deleted.

Two "wherein" clauses have been added. The first requires that at least part of the template is covalently linked to the identifier oligonucleotide, with basis at P3, L27-29. The second requires that chemical entities are reacted under conditions wherein the identifier polynucleotide is at least essentially single stranded, with basis at P3, L1-6 and 29-30. The term "at least essentially single stranded" is defined at P3, L33-P4, L2.

Basis for the amendment to claim 124 is likewise found at P3, L1-6, 12-31.

Claim 130 already contemplates covalent linkage, see steps (iii) and (iv), but a typographical error has been corrected.

2. Non-obviousness

Claims 1, 7, 9, 14, 15, 24, 26, 29, 68, 71, 91, 124, 126, 130 and 131 are rejected under U.S.C. 103(a) as being unpatentable over Liu et al. (US20030113738). The remaining pending claims have been withdrawn from consideration. The independent claims are claims 1, 124, and 130.

The independent claims with the amendments cited herein above are all limited to the situation where there is a covalent linkage between individual building block oligonucleotides. Claim 1 cites "covalently linking said anti-codons", and this same feature is also present in claims 124 and 130, although the wording is a bit different. In claim 124, the anti-codons are referred to as "building block oligonucleotides" (step vi) while in claim 130 they are called "identifier oligonucleotides" (step iii).

Applicant submits that the covalent linkage of building block oligonucleotides and the advantageous effect of this linkage render the claims non-obvious in view of Liu et al.

Generally, the present invention makes it possible to achieve new types of reaction chemistries for templated reaction schemes. As cited at page 3 of the description, the invention makes it possible to generate an essentially single stranded identifier polynucleotide to which a plurality of chemical entities are attached, and react said chemical entities while the identifier polynucleotide is on a single stranded form, thereby enhancing the reactive proximity of

several chemical entities and thereby in turn enhance the formation of a molecule resulting from the reaction of said chemical entities. Furthermore, as the conditions for reaction of the chemical entities are not limited to reaction conditions allowing for hybridisation of codons and anti-codons to occur, the types of reaction chemistries which can be pursued in accordance with the present invention have been increased significantly.

Covalent linkage of individual building block oligonucleotides is one way of ensuring that the chemical entities of the building blocks remain within reactive proximity when the oligonucleotides of the building blocks have been separated from the template, thus generating an at least partly single stranded identifier polynucleotide associated with a plurality of chemical entities.

Liu et al. discloses compositions and methods for synthesizing, selecting, amplifying and evolving non-natural molecules based on nucleic acid templates. In particular, Liu et al. discloses a method comprising the steps of (cf. p. 2, paragraph [0007]):

i) providing one or more nucleic acid templates,

ii) contacting said template(s) with one or more transfer units comprising

   a. an anti-codon hybridising to a sequence of the template, and

   b. a reactive unit including a building block of the compound to be synthesized,

iii) hybridising said anti-codon(s) to said template(s) in a sequence specific-manner, and

iv) synthesizing the compound by reaction of the reactive units of the transfer units.

It appears essential to the method of Liu et al. that the anti-codons of the transfer units are hybridised to the template during reaction of the reactive units, since otherwise the individual transfer units would not be in reactive proximity. This is further illustrated by the disclosure of Liu et al. p. 6, paragraph [0081] and by the detailed discussion at p. 24, paragraphs [0182] - [0184]. The latter specifically states that "[t]he development of evolvable synthetic small molecule libraries relies on chemical catalysis provided by **the proximity of DNA hybridized reactants**" (p. 24, paragraph [0182], emphasis added). Paragraphs [0182] and [0183] goes on to discuss the importance of constructing the template in a manner allowing for "acceptable distances between hybridized reactants". In other words, it is central to the methods disclosed by Liu et al. that the template is constructed in a manner causing the transfer units hybridised thereto to be in a special configuration, i.e. proximity, allowing for reaction between the reactive units.

Furthermore, although this is not specifically discussed in Liu et al., the prerequisite of hybridisation between template and transfer units significantly limits the possible reaction conditions. In particular, it is essential to the method of Liu et al. that the reaction conditions under which the individual reactive units react to form a compound are compatible with continued hybridisation of template and transfer units.

In contrast to the method of Liu et al., the present invention provides a method wherein template is separated from one or more of the anti-codons of the building blocks hybridised thereto prior to reaction of the chemical entities of individual building blocks. If such a separation was

performed in the method of Liu et al., the reaction between reactive units would be impossible, since the reactive units would no longer be held in reactive proximity by their hybridisation, via the anti-codon, to the template. In the present invention, the covalent linkage of the anti-codons of the building blocks makes it possible to keep the chemical entities in reactive proximity even after the template has been separated from the anti-codons of the building blocks. Thus, in combination with the covalent linkage of anti-codons of individual building blocks, the said separation leads to generation of an at least partly single stranded identifier polynucleotide associated with a plurality of chemical entities, wherein said chemical entities may react to form an encoded molecule.

In conclusion, applicant submits that non-obviousness should be acknowledged for claims 1, 124 and 130 in this respect.

Claims 7, 9, 14, 15, 24, 26, 29, 68, 71 and 91 depend on claim 1. Claim 126 depends on claim 124. Claim 131 depends on claim 130. Accordingly, non-obviousness should be acknowledged for these claims.

3. Unity

Since claims 1, 124 and 130 are allowable, all dependent claims should be rejoined pursuant to MPEP 821.04 and PCT Rule 13.1. All withdrawn claims are directly or indirectly dependent on 1, 124 or 130.

Respectfully submitted,

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